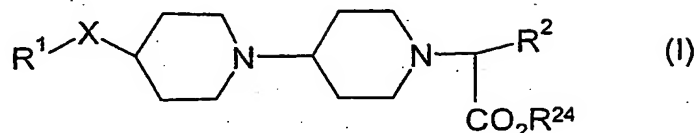


CLAIMS

1. A compound of formula (I):



wherein:

X is CH<sub>2</sub>, C(O), O, S, S(O), S(O)<sub>2</sub> or NR<sup>3</sup>;

R<sup>1</sup> is hydrogen, C<sub>1-6</sub> alkyl, aryl or heterocyclyl;

R<sup>2</sup> is C<sub>3-7</sub> cycloalkyl {optionally substituted by C<sub>1-4</sub> alkyl, aryl or oxo}, C<sub>3-7</sub>

cycloalkenyl {optionally substituted by oxo, C<sub>1-6</sub> alkyl or aryl}, aryl or

heterocyclyl;

wherein the foregoing aryl and heterocyclyl moieties are optionally substituted by:

halogen, cyano, nitro, hydroxy, oxo, S(O)<sub>p</sub>R<sup>4</sup>, OC(O)NR<sup>5</sup>R<sup>6</sup>, NR<sup>7</sup>R<sup>8</sup>, NR<sup>9</sup>C(O)R<sup>10</sup>,

NR<sup>11</sup>C(O)NR<sup>12</sup>R<sup>13</sup>, S(O)<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, NR<sup>16</sup>S(O)<sub>2</sub>R<sup>17</sup>, C(O)NR<sup>18</sup>R<sup>19</sup>, C(O)R<sup>20</sup>, CO<sub>2</sub>R<sup>21</sup>,

NR<sup>22</sup>CO<sub>2</sub>R<sup>23</sup>, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> alkoxy(C<sub>1-6</sub>)alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub>

haloalkoxy, C<sub>1-6</sub> alkoxy(C<sub>1-6</sub>)alkoxy, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> haloalkylthio, C<sub>2-6</sub> alkenyl,

C<sub>2-6</sub> alkynyl, C<sub>3-10</sub> cycloalkyl (itself optionally substituted by C<sub>1-4</sub> alkyl or oxo),

methylenedioxy, difluoromethylenedioxy, phenyl, phenyl(C<sub>1-4</sub>)alkyl, phenoxy,

phenylthio, phenyl(C<sub>1-4</sub>)alkoxy, heterocyclyl, heterocyclyl(C<sub>1-4</sub>)alkyl,

heterocyclioxy or heterocyclyl(C<sub>1-4</sub>)alkoxy; wherein any of the immediately

foregoing phenyl and heterocyclyl moieties are optionally substituted with halogen,

hydroxy, nitro, S(O)<sub>q</sub>(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>NH<sub>2</sub>, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy,

C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl), C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join

to form a ring as described for R<sup>5</sup> and R<sup>6</sup> below), CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-4</sub> alkyl),

NHC(O)(C<sub>1-4</sub> alkyl), NHS(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), C(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub> or OCF<sub>3</sub>;

p and q are, independently, 0, 1 or 2;

R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>21</sup> and R<sup>22</sup> are,

independently, hydrogen, C<sub>1-6</sub> alkyl (optionally substituted by halogen, hydroxy or

C<sub>3-10</sub> cycloalkyl), CH<sub>2</sub>(C<sub>2-6</sub> alkenyl), phenyl (itself optionally substituted by

halogen, hydroxy, nitro, NH<sub>2</sub>, NH(C<sub>1-4</sub> alkyl), N(C<sub>1-4</sub> alkyl)<sub>2</sub>, S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl),

S(O)<sub>2</sub>NH<sub>2</sub>, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl),

C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for

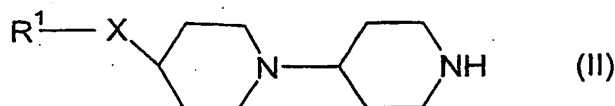
$R^5$  and  $R^6$  below),  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHC}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHS}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{CF}_3$  or  $\text{OCF}_3$ ) or heterocyclyl (itself optionally substituted by halogen, hydroxy, nitro,  $\text{NH}_2$ ,  $\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{N}(\text{C}_{1-4} \text{ alkyl})_2$ ,  $\text{S}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{NH}_2$ ,  $\text{S}(\text{O})_2\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  below), cyano,  $\text{C}_{1-4} \text{ alkyl}$ ,  $\text{C}_{1-4} \text{ alkoxy}$ ,  $\text{C}(\text{O})\text{NH}_2$ ,  $\text{C}(\text{O})\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  below),  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHC}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHS}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{CF}_3$  or  $\text{OCF}_3$ ); alternatively  $\text{NR}^5\text{R}^6$ ,  $\text{NR}^7\text{R}^8$ ,  $\text{NR}^{12}\text{R}^{13}$ ,  $\text{NR}^{14}\text{R}^{15}$ ,  $\text{NR}^{18}\text{R}^{19}$ , may, independently, form a 4-7 membered heterocyclic ring, azetidine, pyrrolidine, piperidine, azepine, 1,4-morpholine or 1,4-piperazine, the latter optionally substituted by  $\text{C}_{1-4}\text{alkyl}$  on the distal nitrogen;

$R^4$ ,  $R^{17}$  and  $R^{23}$  are, independently,  $\text{C}_{1-6} \text{ alkyl}$  (optionally substituted by halogen, hydroxy or  $\text{C}_{3-10} \text{ cycloalkyl}$ ),  $\text{CH}_2(\text{C}_{2-6} \text{ alkenyl})$ , phenyl (itself optionally substituted by halogen, hydroxy, nitro,  $\text{NH}_2$ ,  $\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above),  $\text{S}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{NH}_2$ ,  $\text{S}(\text{O})_2\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above), cyano,  $\text{C}_{1-4} \text{ alkyl}$ ,  $\text{C}_{1-4} \text{ alkoxy}$ ,  $\text{C}(\text{O})\text{NH}_2$ ,  $\text{C}(\text{O})\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above),  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHC}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHS}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{CF}_3$  or  $\text{OCF}_3$ ) or heterocyclyl (itself optionally substituted by halogen, hydroxy, nitro,  $\text{NH}_2$ ,  $\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above),  $\text{S}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{NH}_2$ ,  $\text{S}(\text{O})_2\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{S}(\text{O})_2\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above), cyano,  $\text{C}_{1-4} \text{ alkyl}$ ,  $\text{C}_{1-4} \text{ alkoxy}$ ,  $\text{C}(\text{O})\text{NH}_2$ ,  $\text{C}(\text{O})\text{NH}(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})\text{N}(\text{C}_{1-4} \text{ alkyl})_2$  (and these alkyl groups may join to form a ring as described for  $R^5$  and  $R^6$  above),  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHC}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{NHS}(\text{O})_2(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{C}(\text{O})(\text{C}_{1-4} \text{ alkyl})$ ,  $\text{CF}_3$  or  $\text{OCF}_3$ );

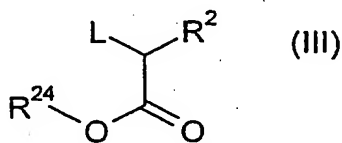
$R^{24}$  is hydrogen,  $\text{C}_{1-6} \text{ alkyl}$  or benzyl; or an N-oxide thereof; or a pharmaceutically acceptable salt thereof; or a solvate thereof.

2. A compound of formula (I) as claimed in claim 1 wherein X is O.
3. A compound of formula (I) as claimed in claim 1 or 2 wherein  $R^{24}$  is hydrogen.
- 5 4. A compound of formula (I) as claimed in claim 1, 2 or 3 wherein  $R^1$  is phenyl optionally substituted with fluorine, chlorine,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkoxy.
5. A compound of formula (I) as claimed in claim 1, 2, 3 or 4 wherein  $R^2$  is phenyl or heterocyclyl, either of which is optionally substituted by: halo, hydroxy, nitro,  
10 cyano, amino,  $C_{1-4}$  alkyl (itself optionally substituted by  $S(O)_2(C_{1-4}$  alkyl) or  $S(O)_2$ phenyl),  $C_{1-4}$  alkoxy,  $S(O)_pR^4$  (wherein p is 0, 1 or 2),  $C(O)NH_2$ ,  $NHS(O)_2(C_{1-4}$  alkyl),  $S(O)_2NH_2$ ,  $S(O)_2NH(C_{1-4}$  alkyl) or  $S(O)_2N(C_{1-4}$  alkyl) $_2$ ; and  $R^4$  is  $C_{1-4}$  alkyl,  $C_{1-4}$  hydroxyalkyl,  $C_{3-7}$  cycloalkyl or  $C_{3-7}$  cycloalkyl( $C_{1-4}$  alkyl).
- 15 6. A process for preparing a compound of formula (I) as claimed in claim 1, the process comprising:

- i. coupling a compound of formula (II):

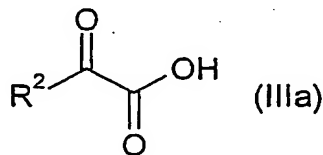


with a compound of formula (III):



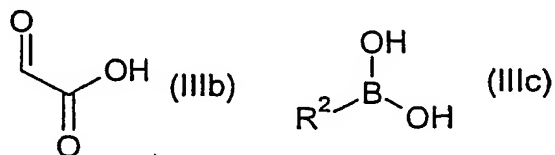
wherein L is a suitable leaving group, in a suitable solvent; or,

- ii. reductive amination of a compound (II) with an ester compound of formula (IIIa):



in the presence of  $NaBH(OAc)_3$  and acetic acid, followed optionally by removal of the ester group; or

- iii. a three component coupling of a compound of formula (II) with compounds of formula (IIIb) and (IIIc):



- 5      7. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, and a pharmaceutically acceptable adjuvant, diluent or carrier.
- 10      8. A compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, for use in therapy.
- 15      9. A compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, in the manufacture of a medicament for use in therapy.
- 20      10. A method of treating a chemokine mediated disease state in a mammal suffering from, or at risk of, said disease, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1.